

REMARKS

Claims 15, 16, 18, and 20-42 are pending in the present application.

At the outset, Applicants wish to thank Examiner Nashed for the very detailed and thorough Office Action and examination of the present application.

In addition, Applicants wish to thank Examiner Nashed for the indication that Claims 20-22 would be allowable if amended to identify the protein in the crystal by sequence identification number, remove the parenthetical phrase, and to replace certain words (see page 14 of the Office Action mailed July 8, 2004). To this end, Applicants have amended these claims to insert the appropriate sequence identification number and to remove the parenthetical phrase. However, with respect to the terms "hexagonal system," "rhombohedral system" and "trigonal system," Applicants submit that these are technical terms conventionally used to represent crystal structures. As such, these terms would be widely appreciated in the relevant art and need not be amended.

Reconsideration of the outstanding rejections and allowance of the pending claims is requested in view of the amendments and remarks set forth herein.

The rejections of: (a) Claims 19-22 under 35 U.S.C. §112, first paragraph (written description), and (b) Claims 1-4, 17, and 19-27 under 35 U.S.C. §112, first paragraph (enablement), are believed to be obviated by amendment.

The apparent basis for this ground of rejection appears to be the Examiner's assertion that the claims as originally presented relate to "all possible crystals of any, presumably, protein having any transphosphorylation activity and/or phosphatase activity... any crystal of *Escherichia blattae* acid phosphatase and mutants thereof..." To address this criticism by the

Examiner, Applicants have amended the claims to incorporate each sequence identification number for the mutant enzymes. Applicants note that the sequences to be mutated have been added in the substitute Sequence Listing as SEQ ID NOs: 124 and 125 and originally appeared in Figure 9.

Applicants submit that the claims as present herein above are in full compliance with 35 U.S.C. §112, first paragraph. As such, Applicants request withdrawal of these grounds of rejection.

The rejection of Claims 1-17 and 19-27 under 35 U.S.C. §112, second paragraph, are traversed in part and obviated in part.

Applicants note that the claims have been substantially rewritten to address the Examiner's several points of criticism. For example, the claims have been amended to clearly indicate that phrases such as "the 61st leucine residue" is intended to relate to the 61st residue in SEQ ID NO: 125 (i.e., Leu-61) and not the 61st occurrence of the leucine therein. Incidentally, Applicants wish to thank the Examiner for the helpful suggestions for rewriting the claims.

However, as stated above with respect to the terms "hexagonal system," "rhombic system" and "trigonal system," Applicants submit that these are technical terms conventionally used to represent crystal structures. As such, these terms would be widely appreciated in the relevant art and need not be amended.

In view of the foregoing, Applicants believe that the language of the claims are such that a person of ordinary skill in the art could interpret the metes and bound of the claims so as to understand how to avoid infringement (MPEP §2173.02). Since the skilled artisan can readily appreciate the meaning of the claims, Applicants submit that further amendments are

unnecessary. Therefore, Applicants request withdrawal of the claim rejection pursuant to MPEP §2173.02.

Acknowledgement that this ground of rejection has been withdrawn is requested.

The rejections of Claims 1-14, 17, and 23-27 under: (a) 35 U.S.C. §102(b) over Mihara et al (EP0857788A2); (b) 35 U.S.C. §102(e) over any of U.S. 6,015,697, U.S. 6,207,435, and U.S. 6,355,472, each to Mihara et al; and (c) 35 U.S.C. §102(b) and (e) over Mihara et al (EP0832970) and Mihara et al (U.S. 6,010,851), are obviated by amendment.

Applicants note that Claims 1-14 and 17 have been canceled. Claims 23-27 (and new Claims 28-42) have been amended to depend from Claims 15 and 16, which the Examiner recognizes as being free from the aforementioned references. As such, these grounds of rejection are believed to be no longer tenable.

Withdrawal of these grounds of rejection is requested.

The rejection of Claims 15 and 16 under 35 U.S.C. §103(a) over Mihara et al or any of the corresponding U.S. Patents 6,015,697, 6,207,435, and 6,355,472, is respectfully traversed.

Mihara et al only disclose mutant acid phosphatase from *Enterobacter aerogenes* wherein Gly-92, Glu-112, Thr-169, and Ile-171 have been replaced (see page 6, lines 51-54 of EP 0 857 788 A2). More importantly, the replacements recited in Claim 15 for SEQ ID NO: 125 are not disclosed for *Enterobacter aerogenes*.

Further, the mutant acid phosphatases from *Escherichia blattae* disclosed in Table 12 of the document are only functional-related homologues of a wild type enzyme. The mutant

acid phosphatases of Claim 15 of the present application were obtained based on 3D-structural analysis and have more efficient nucleoside-5'-phosphate-producing ability. Therefore, the mutant acid phosphatase of Claim 15 is not obvious over Mihara et al.

Furthermore, replacement of Glu-102 or Thr-149 is neither disclosed, nor suggested for *Escherichia blattae* in the disclosures of Mihara et al (see Table 12 of Mihara et al). Thus, the mutant acid phosphatase of Claim 16 is not obvious over Mihara et al.

Applicants request withdrawal of this ground of rejection.

The objections to (a) Claim 2 under 37 C.F.R. §1.75(c) and (b) Claims 1-16 as omitting a sequence identification number are obviated by amendment.

Applicants note that Claims 1-14 have been canceled in the present amendment and Claims 15 and 16 have been amended to recite the sequence identification number. As such, these grounds of objection are no longer believed to be applicable.

Withdrawal of these objections is requested.

The objections to the drawings and to the specification are believed to be obviated by the submission of replacement Figure 3 and the amendments herein.

Specifically, new Figure 3 is believed to clearly show the binding site of the nucleoside phosphate. Further, the specification has been amended to remove the hyperlink and to define the sequences appearing in Figures 1, 2, and 9.

In addition, in view of the Examiner's indication that the Sequence Listing filed on July 25, 2001, does not contain all the disclosed sequences, Applicants submit herewith a substitute Sequence Listing in which SEQ ID NOs: 124 and 125 have been added corresponding to the sequences appearing in Figure 9. Applicants also submit herewith a

corresponding computer-readable Sequence Listing. The sequence information recorded in the corresponding computer-readable Sequence Listing is identical to the paper copy of the substitute Sequence Listing. Support for all of the sequences listed in the substitute Sequence Listing is found in the present application and the Sequence Listing as originally filed. The submission of the substitute Sequence Listing and the corresponding computer-readable Sequence Listing have introduced no new matter.

Applicants also note that the Examiner has specifically pointed to page 2, last paragraph as failing to “identify a disclosed amino acid sequences by a specific sequence identification number at each occurrence.” However, this assertion is incorrect as the only specifically disclosed sequences appearing in this paragraph are at page 3, lines 1-2, which explicitly recite the corresponding sequence identification number. Therefore, no further amendment is necessary.

The Figure legend for Figure 2 has been amended to indicate the corresponding sequence identification numbers for each sequence recited therein. In addition, the claims have been amended, as appropriate, to specifically indicate the appropriate sequence identification numbers.

In regard to the Examiner’s indication that Examples 1-3 must be amended to introduce sequence identification numbers at each occurrence where the proteins are mentioned, Applicants remind the Examiner that sequence identification numbers are only necessary where a sequence is explicitly disclosed (37 C.F.R. §1.821-1.825). Examples 1-3 do not contain such an explicit disclosure. As such, no amendment is believed to be necessary.

As for the use of the term "Explanation" appearing at page 30, line 19, Applicants have amended the same in accordance with the Examiner's suggestion. Namely, the specification has been amended to insert the term "Description."

The specification is now believed to be proper. An indication that the objection to the drawings and to the specification have been withdrawn is requested.

The Examiner has required restriction in the present application as follows:

- Group I: Claims 1-17 and 19-27, drawn to mutant of nucleoside-5'-phosphate producing enzyme, crystal, method of making mutants using atomic coordinates (first use), and nucleic acid encoding mutants, and
- Group II: Claim 18, drawn to a method for producing inhibitor utilizing atomic coordinates (second use).

Applicant affirms the election of Group I, with traverse.

Applicants traverse the Restriction Requirement on the grounds that the Office has failed to show that a burden would exist in searching all the claims of the present application.

MPEP §803 states:

If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to independent and distinct inventions.

Applicants submit that a search and examination of all the claims would not constitute a series burden upon the Examiner.

Accordingly, and for the reasons presented above, Applicants submit that the Office has failed to meet the burden necessary in order to sustain the Restriction Requirement. Withdrawal of the Restriction Requirement is respectfully requested.

Finally, the Examiner has issued the following obviousness double-patenting rejections:

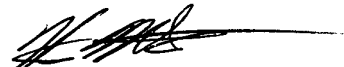
- (a) Claims 1-16 over Claims 1-3 of U.S. 6,207,435;
- (b) Claims 23-25 over Claims 1-5 of U.S. 6,355,472;
- (c) Claims 26 and 27 over Claims 1-14 of U.S. 6,015,697; and
- (d) Claims 1-14 and 23-27 over Claims 1-6, 8, 9, 11, 13, 14, 16, 18, 19, 21, 23, 24, and 26 of U.S. 6,010,851.

Applicants request that the Office hold these obviousness double-patenting rejections in abeyance until such a time as allowable subject matter has been identified in the present application. If necessary, a terminal disclaimer will be filed at that time. Until such a time, Applicants make no statement with respect to the propriety of these grounds of rejection.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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AMENDMENTS TO THE DRAWINGS

The Examiner indicated objections to the drawings (Figures 1-3 and 9) filed on May 3, 2001. Figures 1, 2, and 9 are addressed elsewhere herein. The replacement drawing for Figure 3 filed herewith is believed to contain all of the necessary corrections.

Attachment: Letter Submitting Drawing Sheet(s) / One (1) Replacement Drawing